

## Correspondence

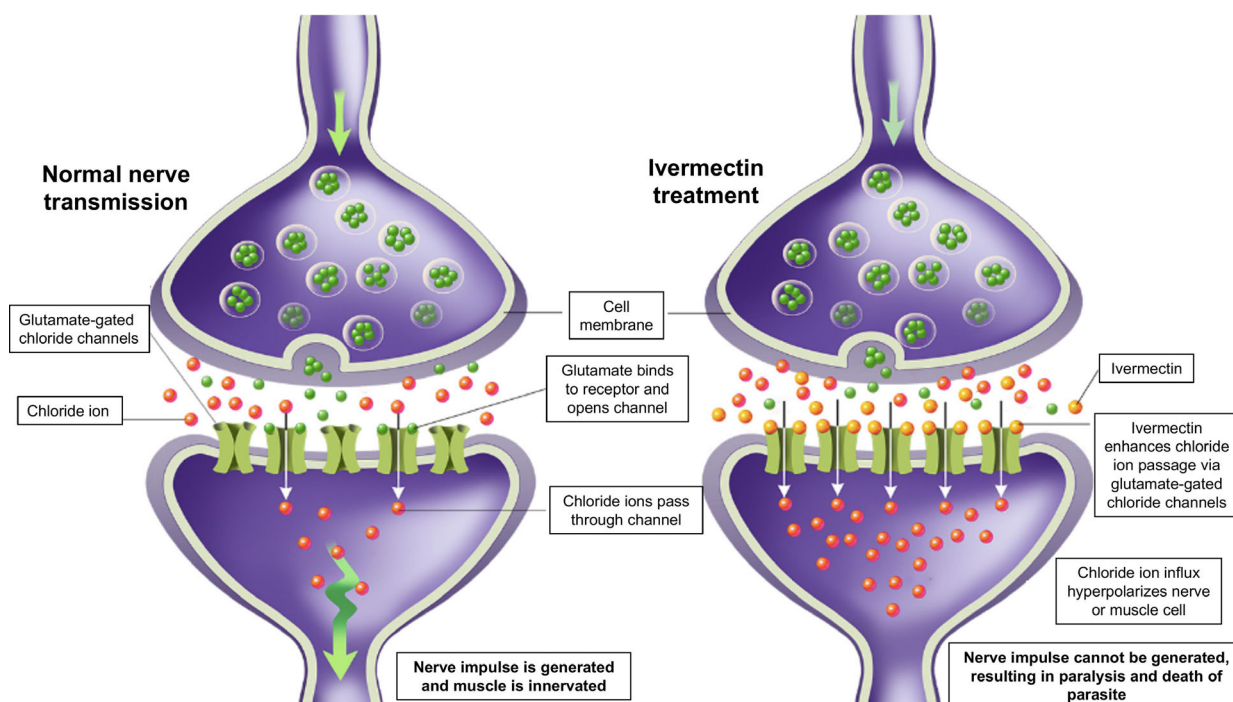
### Ivermectin in dermatology: why it 'mite' be useless against COVID-19

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Misinformation has been a major global challenge in the COVID-19 pandemic. Several therapies relevant to dermatology, including hydroxychloroquine<sup>1</sup> and ultraviolet radiation,<sup>2</sup> have been falsely touted as beneficial. More recently, ivermectin has been advocated for both prophylaxis and treatment of COVID-19. Although ivermectin has been shown to inhibit the replication of severe acute respiratory syndrome coronavirus (SARS-CoV)-2 at supratherapeutic doses *in vitro*,<sup>3</sup> no benefit has been seen in real-world treatment of COVID-19.<sup>4</sup> We review the basic pharmacology of ivermectin, its clinical applications in dermatology, and explain why it is unlikely to be useful against SARS-CoV-2.

Ivermectin is a synthetic derivative of a class of anti-parasitics known as avermectins, discovered by the Irish Nobel Prize winner William Campbell in 1978. Ivermectin has broad-spectrum activity against a variety of endoparasites and ectoparasites. It selectively binds to parasitic neurotransmitter receptors, inducing paralysis in the targeted parasite. It blocks trans-synaptic chemical transmission through glutamate-gated anion channels (Fig. 1), which are not present in vertebrates. At higher concentrations, ivermectin can interact with other ligand-gated chloride channels.

Ivermectin is approved to treat several parasitic infestations with cutaneous tropism, in both oral and topical formulation (Table 1). It is commonly used in the treatment of resistant or crusted scabies, as a second-line strategy in cases of suspected permethrin resistance, or when topical treatment is not feasible. Ivermectin also



**Figure 1** Mechanism of action comparing a normal parasitic nerve synapse and a parasitic nerve synapse inhibited by ivermectin. Ivermectin induces hyperpolarization of the neuron and death of the parasite.

**Table 1** Dermatological indications for oral and topical ivermectin therapy.

Oral
Scabies
Pediculosis
Demodicosis
Cutaneous larva migrans and cutaneous larva currens
Myiasis, filariasis, onchocerciasis, and loiasis
Topical
Papulopustular rosacea

has activity against human body, head and pubic lice. *Demodex folliculorum*, a human skin commensal, can cause facial or disseminated demodicidosis, and is responsive to ivermectin. Ivermectin is also commonly used in a topical formulation to treat papulopustular rosacea, given the role of *Demodex* in the pathophysiology of this condition. Cutaneous larva migrans and cutaneous larva currens can be treated with single-dose ivermectin. Myiasis, filariasis, onchocerciasis and loiasis have varying responses to ivermectin.

Ivermectin has been shown to have *in vitro* antiviral activity against a variety of viruses, including both RNA and DNA viruses.<sup>5</sup> The mechanism considered to be responsible for this antiviral effect is the inhibition of integrase protein and importin  $\alpha/\beta$ 1 heterodimer, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host's antiviral response.<sup>5</sup> In addition, ivermectin docking may interfere with the attachment of the SARS-CoV-2 spike protein to the human cell membrane.<sup>5</sup> However, the concentration of drug needed to kill viruses *in vitro* is up to 100 times higher than the concentration of ivermectin normally used *in vivo* to control parasitic disease in humans. Some studies of ivermectin have reported potential anti-inflammatory properties, which may be beneficial in people with COVID-19.<sup>5</sup>

Ivermectin is generally a safe and efficacious therapy for its dermatological indications. However, despite

reported antiviral effects at supratherapeutic doses *in vitro*, there is neither clinical evidence nor a plausible biological mechanism to support ivermectin as an effective prophylactic or therapeutic agent against SARS-CoV-2. It is important that healthcare professionals understand the lack of evidence for its application to COVID-19, and continue to refute and rebut misleading health information.

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Conflict of interest: the authors declare that they have no conflicts of interest.

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